

AMENDMENTS

Claims:

Please amend the claims as indicated hereafter.

DRAFT

1. (Previously canceled)
2. (Previously Amended) The method according to claim 37, wherein the primer is a fragment of deoxyribonucleic or ribonucleic acid, an oligodeoxyribonucleotide, an oligoribonucleotide, or a copolymer of deoxyribonucleic acid and ribonucleic acid.
3. (Previously Amended) The method according to claim 37, wherein the nucleic acid of interest is deoxyribonucleic acid, a ribonucleic acid, or a copolymer of deoxyribonucleic acid and ribonucleic acid.
4. (Canceled).
5. (Previously Amended) The method according to claim 37, wherein the terminator nucleotide is a dideoxyribonucleotide or an analogue thereof and the non-terminator nucleotide is a deoxyribonucleotide or a ribonucleotide or an analogue thereof.
6. (Canceled).
7. (Canceled).
8. (Previously Amended) The method according to claim 37, wherein in step (d), the duplex from step (c) is contacted with non-terminator nucleotides, wherein each non-terminator is labeled with the same or different detectable marker.
9. (Previously Amended) The method according to claim 37, wherein said detectable

36. (Presently amended) The method according to claim 2728, wherein the organism
is a human being.

DRAFT

37. (Currently amended) A method for detecting or quantifying the presence of a nucleic acid of interest having a variant of a known target nucleotide base in a predetermined position of a known nucleic acid in a sample by detecting a signal from a plurality of labeled nucleotides incorporated into a primer extension product comprising:

- (a) selecting obtaining a nucleic acid of interest having a target nucleotide base at [[a]] the predetermined position in a template of [[a]] the nucleic acid of interest, wherein the target nucleotide base is a mutant nucleotide base or a known wild type nucleotide base;
- (b) preparing an unlabeled primer complementary to a sequence immediately upstream of the target nucleotide base;
- (c) treating a sample containing the nucleic acid of interest, if the nucleic acid is double-stranded, so as to obtain unpaired nucleotide bases spanning the predetermined position, or directly employing step (d) if the nucleic acid of interest is single-stranded;
- (d) annealing the primer from (b) with the nucleic acid of interest from (c) to obtain a primer-nucleic acid duplex, wherein the target nucleotide base in the nucleic acid of interest is the first unpaired base immediately downstream of the 3' end of the primer;
- (e) mixing the primer-nucleic acid duplex from (d) with a primer extension reaction reagent comprising: (i) three types of non-terminator nucleotides that are not complementarily matched to the known wild type target nucleotide base in the predetermined position of the nucleic acid of interest, wherein at least one type of the non-terminator nucleotide

DRAFT

USSN 09/618,129

Response with Amendments

is labeled with a detectable marker; and optionally (ii) one type of terminator nucleotide that is complementarily matched to the known ~~wild-type target~~ nucleotide base in the predetermined position of the nucleic acid of interest, wherein the terminator nucleotide is not labeled;

(f) extending the primer extension reaction by enzymatic or chemical means to form a labeled primer extension product comprising a plurality of labeled non-terminator nucleotides, wherein a labeled primer extension product does not form when the target nucleotide base in the predetermined position of the nucleic acid of interest is the same as the known target nucleotide base in the predetermined position of the known nucleic acid wild-type; and

(g) determining the presence of the mutant nucleic acid of interest having the variant target nucleotide base at the predetermined position in the nucleic acid of interest by detecting the presence of the labeled primer extension product, wherein detecting the labeled primer extension product is not based on size.

38. (Canceled)

39. (Currently amended) A method for detecting the presence of a nucleic acid having a variant of a known nucleotide base at a predetermined position, comprising:

providing a nucleic acid having a ~~known wild-type target nucleotide base or a mutant target nucleotide base at [[a]]~~ the predetermined position;

annealing a primer to the nucleic acid immediately 3' of the predetermined position; extending the primer in ~~one~~ an extension reaction to form a labeled primer extension product using a reaction mixture comprising non-terminator nucleotides, wherein ~~at least one the~~ non-terminator nucleotide is nucleotides are not complementarily matched to the ~~mutant known~~ nucleotide base at the predetermined position target nucleotide and at least one non-terminator

DRAFT

USSN 09/618,129
Response with Amendments

nucleotide is labeled with a detectable marker; and wherein a labeled primer extension product does not form when the target nucleotide base is the same as the known nucleotide base at the predetermined position wild-type; and

detecting the presence of the labeled primer extension product; and

correlating the presence of the labeled primer extension product with the presence of a mutant target a nucleic acid having a variant of the known nucleotide base at the predetermined position in the nucleic acid.

40. (Currently amended) A method for detecting the presence of a mutant nucleotide in a nucleic acid having a known nucleotide at a predetermined position, comprising:

providing a nucleic acid sample having the nucleic acid with a known wild-type target nucleotide base or a mutant target nucleotide base at [[a]] the predetermined position;

annealing a primer to the nucleic acid immediately 3' of the predetermined position;

extending the primer to form a labeled primer extension product using a reaction mixture comprising non-terminator nucleotides, wherein at least one non-terminator nucleotide is that are not complementarily matched to the known wild-type target nucleotide base at the predetermined position and at least one non-terminator nucleotide is labeled with a detectable marker; and wherein a labeled primer extension product does not form when the identity of the target nucleotide base is mutant is the same as the known nucleotide base at the predetermined position; and

detecting the presence of the labeled primer extension product, wherein the absence of a detectable detection of the labeled primer extension product is not based on the size of the labeled extension product, and wherein detecting a labeled primer extension product indicates the presence of a wild-type the known nucleotide base at the predetermined position in the nucleic

acid.

DRAFT

41. (Currently amended) A method for detecting or quantifying the presence of a known target nucleic acid in a sample by detecting a signal from a plurality of labeled nucleotides incorporated into a primer extension product comprising:

- (a) selecting a nucleic acid having a target nucleotide base at a predetermined position in a template of a nucleic acid of interest, ~~wherein the target nucleotide base is a known mutant nucleotide base or a known wild-type nucleotide base;~~
- (b) preparing an unlabeled primer complementary to a sequence immediately upstream of the target nucleotide base;
- (c) treating a sample containing the nucleic acid of interest, if the nucleic acid is double-stranded, so as to obtain unpaired nucleotide bases spanning the predetermined position, or directly employing step (d) if the nucleic acid of interest is single-stranded;
- (d) annealing the primer from (b) with the nucleic acid of interest from (c) to obtain a primer-nucleic acid duplex, wherein the target nucleotide base in the nucleic acid of interest is the first unpaired base immediately downstream of the 3' end of the primer;
- (e) mixing the primer-nucleic acid duplex from (d) with a primer extension reaction reagent comprising: (i) ~~at least one type of~~ non-terminator nucleotides that are not complementarily matched to the known ~~mutant~~ target nucleotide base, wherein at least one type of the non-terminator nucleotide is labeled with a detectable marker; and optionally (ii) one type of terminator nucleotide that is complementarily matched to the known ~~mutant~~ target nucleotide base, wherein the terminator nucleotide is not labeled;
- (f) extending the primer extension reaction by enzymatic or chemical means to form a labeled primer extension product comprising a plurality of labeled non-terminator nucleotides,

wherein a labeled primer extension product does not form when the target nucleotide base is the
DRAFT
known nucleotide mutant; and

(g) wherein the absence of a detectable primer extension product indicates
determining the presence of the known wild-type target nucleotide at the predetermined position
in the nucleic acid of interest by detecting the presence of the labeled nucleotide in primer
extension product, wherein detecting the labeled nucleotide primer extension product is not
based on size.